UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/088,341	06/25/2002	David Michael Shaw	117-385	9257

23117 7590 02/10/2006

NIXON & VANDERHYE, PC
901 NORTH GLEBE ROAD, 11TH FLOOR
ARLINGTON, VA 22203

EXAMINER	
DEVI, SARVAMANGALA J N	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 02/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/088,341	SHAW ET AL.	
	Examiner	Art Unit	
	S. Devi, Ph.D.	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-10,12,13,15-18 and 20-46* is/are pending in the application.

4a) Of the above claim(s) *26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10,12,13,15-18,20-25 and 31-46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendments

1) Acknowledgment is made of Applicants' amendments filed 07/25/05, 08/05/05 and 10/28/05 in response to the non-final Office Action mailed 03/23/05. Applicants have amended the specification and the claims.

Status of Claims

2) Claims 1-7, 9, 12, 13, 15, 16, 18, 20-24 and 32 have been amended via the amendment filed 07/25/05.

New claims 33-46 have been added via the amendment filed 07/25/05.

Claims 1, 4-6, 9 and 13 have been amended via the amendment filed 07/25/05.

Claims 11, 14 and 19 have been canceled via the amendment filed 07/25/05.

Claims 1, 3-6 and 9 have been amended via the amendment filed 10/28/05.

Claims 1-10, 12, 13, 15-18 and 20-46 are pending.

Claims 1-10, 12, 13, 15-18, 20-25 and 31-46 are under examination.

Prior Citation of Title 35 Sections

3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Objection(s) to Specification

5) The instant specification is objected to for the following reasons:

(a) The specification is objected to for failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP 608.01(o).

Claims 1, 3, 4, 6, 9, 13 and 18, as amended currently, include the added limitation: 'in ... subject to whom the vaccine is administered', which lacks antecedent basis in the specification.

(b) The paragraph inserted at line 16 of page 6 of the specification via the amendment

filed 07/25/05 is objected to under 35 U.S.C. § 132, because it appears to introduce new matter into the disclosure. 35 U.S.C. § 132 states that no amendment shall introduce new matter into the disclosure of the invention.

Applicants point to page 38, line 17 to page 39, line 6 of the specification and state that this section provides support for the inserted/amended paragraph. Applicants state that it is apparent from the third column of each set in Figure 1 that it represents the result for intranasal immunization with *Lactobacillus plantarum* pLP503-TTFC as indicated in the brief description of the drawing and page 38, line 31 to page 39, line 6 of the specification. However, these parts of the specification describe that mice used for oral or intranasal immunization with *Lactobacillus plantarum* pLP503-TTFC are limited to 'C57BL/6 mice'. Furthermore, the added sentence: 'The third bar in each set shows the results for intranasal immunization with *L. plantarum* pLP503-TTFC' lacks descriptive support at 38, line 17 to page 39, line 6 of the specification, as originally filed.

Objection(s) Withdrawn

6) The objection to the specification made in paragraph 7(A) of the Office Action mailed 03/23/05 is withdrawn. A new objection is set forth on the amended specification.

7) The objection to the specification made in paragraph 7(B) of the Office Action mailed 03/23/05 is withdrawn in light of Applicants' amendments.

8) The objection to claim 6 made in paragraph 39 of the Office Action mailed 03/23/05 is withdrawn in light of Applicants' amendment to the claim.

Rejection(s) Moot

9) The rejection of claims 11, 14 and 19 made in paragraph 11 of the Office Action mailed 07/01/04 and maintained in paragraph 31 of the Office Action mailed 03/23/05 under 35 U.S.C. § 102(b) as being anticipated by Pouwels *et al.* (*J. Biotechnol.* 44: 183-192, 1996) (Pouwels *et al.*, 1996) as evidenced by Hoshino *et al.* (*J. Virol.* 62: 744-748, 1988, abstract) or Virelizier JL (*J. Immunol.* 115: 434-439, 1975, abstract), Naidu (US 20020192202 A1) and Wells *et al.* (*Antonie van Lewuwenhoek* 70: 317-330, 1996 - Applicants' IDS) (Wells *et al.*, 1996), is moot in light of Applicants' cancellation of the claims.

10) The rejection of claim 14 made in paragraph 35(g) of the Office Action mailed 03/23/05

under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

11) The rejection of claim 11 made in paragraph 35(i) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

12) The rejection of claim 14 made in paragraph 35(j) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

13) The rejection of claim 19 made in paragraph 35(t) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

14) The rejection of claims 11, 14 and 19 made in paragraph 35(w) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claims.

15) The rejection of claim 19 made in paragraph 35(x) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is moot in light of Applicants' cancellation of the claim.

Rejection(s) Withdrawn

16) The rejection of claim 5 made in paragraph 9(g) of the Office Action mailed 07/01/04 and maintained in paragraph 29 of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

17) The rejection of claim 16 (not claim 15 as mistyped) made in paragraph 9(p) of the Office Action mailed 07/01/04 and maintained in paragraphs 30 and 33 of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

18) The rejection of claims 5 and 9 made in paragraph 34 of the Office Action mailed 03/23/05 under 35 U.S.C § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendment to the claims.

19) The rejection of claims 20 and 22 made in paragraph 12 of the Office Action mailed 07/01/04 and maintained in paragraph 32 of the Office Action mailed 03/23/05 under 35 U.S.C. § 102(b) as being anticipated by Mercenier *et al.* (*Adv. Food Sci.* 18: 73-77, 1996), is withdrawn in light of Applicants' amendment to the base claim to now add the limitation '*plantarum*'.

20) The rejection of claim 1 made in paragraph 35(a) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

21) The rejection of claims 9 and 18 made in paragraph 35(b) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

22) The rejection of claims 3-5 made in paragraph 35(c) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

23) The rejection of claims 1, 2 and 18 made in paragraph 35(d) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

24) The rejection of claim 18 made in paragraph 35(e) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

25) The rejection of claims 2, 3, 7, 12-13 and 18 made in paragraph 35(f) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

26) The rejection of claim 9 made in paragraph 35(h) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

27) The rejection of claim 20 made in paragraph 35(k) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

28) The rejection of claim 20 made in paragraph 35(l) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

29) The rejection of claim 21 made in paragraph 35(m) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

30) The rejection of claim 24 made in paragraph 35(n) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

31) The rejection of claims 5 and 9 made in paragraph 35(o) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claims.

32) The rejection of claim 5 made in paragraph 35(p) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

33) The rejection of claim 13 made in paragraph 35(q) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

34) The rejection of claim 13 made in paragraph 35(r) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

35) The rejection of claim 18 made in paragraph 35(s) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

36) The rejection of claim 22 made in paragraph 35(u) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

37) The rejection of claim 23 made in paragraph 35(v) of the Office Action mailed 03/23/05

under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the claim.

38) The rejection of claims 2-10, 12, 13, 15-17, 31 and 32 made in paragraph 35(w) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

39) The rejection of claims 23 and 25 made in paragraph 35(x) of the Office Action mailed 03/23/05 under 35 U.S.C. § 112, second paragraph, as being indefinite, is withdrawn in light of Applicants' amendment to the base claim.

40) The rejection of claims 1 and 8 made in paragraph 37 of the Office Action mailed 03/23/05 under 35 U.S.C. § 102(a) as being anticipated by Maassen (*J. Immunol. Methods* 223: 131-136, February 1999, already of record), is withdrawn in light of Applicants' amendments to the claims. A modified rejection is set forth below.

41) The rejection of claims 1-6, 9-12, 14, 15, 20, 21, 24, 31 and 32 made in paragraph 38 of the Office Action mailed 03/23/05 under 35 U.S.C. § 102(b) as being anticipated by Madsen *et al.* (WO 98/10079), is withdrawn.

Rejection(s) Maintained

42) The rejection of claims 1-7, 9, 10, 12, 13, 15-18, 20-25, 31 and 32 made in paragraph 11 of the Office Action mailed 07/01/04 and/or maintained in paragraph 31 of the Office Action mailed 03/23/05 under 35 U.S.C. § 102(b) as being anticipated by Pouwels *et al.* (*J. Biotechnol.* 44: 183-192, 1996) (Pouwels *et al.*, 1996) as evidenced by Hoshino *et al.* (*J. Virol.* 62: 744-748, 1988, abstract) or Virelizier JL (*J. Immunol.* 115: 434-439, 1975, abstract), Naidu (US 20020192202 A1) and Wells *et al.* (*Antonie van Lewuwenhoek* 70: 317-330, 1996 - Applicants' IDS) (Wells *et al.*, 1996), is maintained for reasons set forth therein and herebelow.

New claims 35, 37-41, 43, 44 and 46 are now included in this rejection, because Pouwels' (1996) teachings meet the limitations of the new claims explicitly or inherently. See paragraph 11 of the Office Action of June 04 and paragraph 31 of the Office Action of February 05.

Applicants contend that from Figure 4 of Pouwels *et al.*, it is not possible for a skilled person to ascertain which *Lactobacillus* strain was administered. Applicants opine that 'the most likely

strain to have been administered would have been *Lactobacillus casei*'. Applicants state that there is no demonstration that any of the *Lactobacillus plantarum* strains discussed in Pouwels *et al.* would be able to give rise to an immune response when administered orally. Applicants submit that: (a) 'though something may be 'antigenic' (i.e., antibodies may potentially be raised against it), that is not the same as something which is 'immunogenic' (i.e., something which actually gives rise to an immune response when administered)' [Emphasis in original]; (b) Something may be antigenic (i.e., have the ability to be recognized by antibodies) but not be immunogenic (i.e., not actually give rise to an immune response when administered) because of the context or way in which it is administered; (c) Whilst the vast majority of protein sequences are antigenic, it is only when administered in the appropriate context that they are actually immunogenic and give rise to an immune response. A vaccine which is antigenic, but not immunogenic, is a failure because it will not elicit an immune response when administered. With regard to the teachings of Pouwels *et al.*, Applicants state that although the strain described in Pouwels *et al.* may express an antigen against which antibodies can be generated, there is no evidence that they are able to give rise to an immune response when administered orally. Applicants allege that Figure 4 of Pouwels *et al.* does not provide such evidence. Applicants contend that they have amended claims 1, 18, 20 and 22 to clarify that Applicants' vaccines elicit and induce an immune response when administered 'orally'. With regard to the Office's discussion of section 3.5 of Pouwels *et al.*, Applicants submit that all of the strains shown in Figure 4 were incubated for 7 hours and hence it is not possible to tell which strain was actually administered because Pouwels *et al.* only refer to administration of *Lactobacillus* 'which could, and indeed was most likely to have been', *Lactobacillus casei.*

Applicants' arguments have been carefully considered, but are not persuasive. Contrary to Applicants' assertion, the instant specification at page 15, first paragraph, expressly describes that: (a) the 'antigen is able to elicit or stimulate an immune response, and so can be any antigen against which an immune response' can be elicited in an animal; and (b) the 'antigen can be an immunogen'. In the instant application, the limitation 'oral vaccine' in claim 1 for example represents the intended use of the recited recombinant *Lactobacillus plantarum* and therefore has no patentable weight. The structural limitation in claim 1 that is required to be met by the prior art product, structure-wise, is a recombinant *Lactobacillus plantarum* which expresses a heterologous antigen intracellularly and/or

on its surface. The limitation regarding the elicitation of an immune response against the heterologous antigen in a subject to whom the recombinant *Lactobacillus plantarum* is administered, represents the functional limitation. As long as the prior art taught a recombinant *Lactobacillus plantarum* expressing a heterologous antigen intracellularly and/or on its surface, such a recombinant *Lactobacillus plantarum* anticipates the claim(s). Pouwels' (1996) product meets the instantly claimed product structurally. The limitation on the elicitation of an immune response against the heterologous antigen in a subject to whom the vaccine administered, is viewed as an inherent function that is inseparable from the prior art product. Products that are identical in structure or composition cannot have mutually exclusive properties. Such products and their properties are inseparable. Therefore, if the prior art taught the identical product, the property Applicant discloses and/or claims is necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Although Pouwels *et al.* (1996) are silent about the one or more properties recited in the instant claims, the prior art recombinant *Lactobacillus plantarum* expressing the heterologous antigen intracellularly is viewed as the same as the Applicants' recombinant *Lactobacillus plantarum* expressing the heterologous antigen intracellularly, because the prior art product meets all the structural limitations of the claimed product. Since the prior art recombinant *Lactobacillus plantarum* expressing a heterologous antigen is structurally the same as the recombinant *Lactobacillus plantarum* recited in the instant claims, it is expected to have the same intrinsic properties as that of the Applicants' recombinant *Lactobacillus plantarum*, i.e., the ability to elicit an immune response against the heterologous antigen in a subject to whom the vaccine is administered. MPEP 2112.01 [R-3] states that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the Applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Since the Office does not have the facilities for examining and comparing Applicants' recombinant *Lactobacillus plantarum* expressing a heterologous antigen with the prior art recombinant *Lactobacillus plantarum* expressing a heterologous antigen intracellularly for

functional properties, the burden is on the Applicants to show a novel or an unobvious difference between the instantly claimed product and the prior art product. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzerald et al.*, 05 USPQ 594.

With regard to Figure 4 of Pouwels *et al.* (1996), Applicants are correct in that all of the four recombinant *Lactobacilli* were cultivated for 7 h. However, contrary to Applicants' assertion, section 3.5 of Pouwels *et al.* (1996) discloses that *oral* administration of *Lactobacillus* harbouring the *HA-uidA* gene and that were cultivated for 7 h after dilution from an overnight culture, resulted in a significant immune response. The only possible interpretation of this disclosure is that all recombinant *Lactobacilli* that were cultivated for 7 h were orally administered and all induced a significant immune response. It is important to note that of the four recombinant *Lactobacilli* depicted in Figure 4, three are recombinant *Lactobacillus plantarum*, i.e., Lp. 8014, Lp. 14917, and Lp NCIB. Of these, Lp. NCIB and Lp. 8014 showed the highest heterologous antigen expression following 7 h of cultivation. Therefore, from Figure 4 of Pouwels *et al.* (1996), it is impossible for a skilled person to ascertain exclusively that *Lactobacillus casei* strain was the strain that was orally administered. Therefore, the alleged likelihood that only recombinant *Lactobacillus casei* (which clearly did not express as much of the heterologous antigen as did *Lactobacillus plantarum,* NCIB and 8014) was orally administered by Pouwels *et al.* (1996) is not persuasive. There is no convincing evidence in Pouwels' (1996) disclosure or in Applicants' arguments establishing that what was administered orally by Pouwels *et al.* (1996) was recombiannt *L. casei* and not one of the three recombinant *Lactobacillus plantarum.* Moreover, irrespective of which of the three recombinant *Lactobacillus plantarum* and the *Lactobacillus casei* was orally administered by Pouwels *et al.* (1996), as explained above, since elicitation of an immune response in a subject as recited, for example, in claim 1 or claim 18, is a functional limitation, such a function is inherent to Pouwels' (1996) recombinant *Lactobacillus plantarum*, i.e., Lp. 8014, Lp. 14917, and Lp NCIB. As set forth previously, the instant specification specifically defines the term 'oral vaccine' at lines 19 and 20 of page 7 of the specification as any vaccine that is suited, adapted, intended and/or formulated for oral delivery. The instant claims are drawn to a product that is intended to be administered orally, intended for use as a 'oral vaccine', or is formulated for oral delivery as defined by Applicants in the specification. The prior art vaccine of Pouwels *et al.* (1996) meets this

definition. Given that the limitation on the elicitation of an immune response against the heterologous antigen in a subject to whom the vaccine is administered orally is a functional limitation, Pouwels *et al.* (1996) do not even have to teach that their vaccine was orally administered to a subject to be anticipatory. The vaccine claimed, for example in instant claim 1, is only required to comprise a recombinant *Lactobacillus plantarum* that expresses a heterologous antigen intracellularly and/or on its surface and is required be intended for oral administration. For the reasons delineated above, the rejection stands.

New Rejections Based on Applicants' Amendments

The new rejections set forth below are necessitated by Applicants' amendments to the claims and submission of new claims.

Rejection(s) under 35 U.S.C. § 112, First Paragraph (New Matter)

43) Claims 1, 3-6, 9, 13 and 18 and those dependent therefrom are rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The added limitation: 'in a subject to whom the vaccine is administered' in claim 1 or 18 is new matter. The added limitation in claims 3-6, 9 and 13: 'in said subject to whom the vaccine is administered' is new matter. Applicants do not point to a specific part(s) of the specification that provides descriptive support for the added limitations. A review of the specification, as originally filed, indicates that while administration of the vaccine to 'a human or an animal' is supported on page 7 of the specification, the administration of the vaccine to a generic 'subject' is not. In terms of scope, the genus 'subject' is not the same as the subgenus 'human or animal'. The subgenus 'human' or 'animal' does not provide support for the full scope of the generic term 'subject', which encompasses non-human and non-animal subjects. *In re East and Harman* (CCPA) 181 USPQ 716 (May 9, 1974) – claims of a reissue application are drawn to new matter since they broadly recite genus of 'carrier particles' which is not disclosed in original patent, which discloses only subgenus of 'magnetic carrier particles' and species of 'iron, ferrites, nickel, and cobalt' carrier particles. Therefore, the above-identified new limitations in the claim(s) are considered to be new matter. Therefore, the above-identified limitation in the claims is considered to be new matter. *In re*

Rasmussen, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

44) Claim 5 is rejected under 35 U.S.C § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The added limitation '*carnii*' in claim 5 is new matter, because there appears to be no descriptive support in the specification, as originally filed, for this new limitation. Therefore, the above-identified limitation in the claim is considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are respectfully requested to point to the descriptive support in the specification as filed, for the newly added limitation(s), or to remove the new matter from the claim(s).

Rejection(s) under 35 U.S.C. § 112, Second Paragraph

45) Claims 1-10, 12, 13, 15-18, 20-25 and 31-46 are rejected under 35 U.S.C § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 18, as amended, is indefinite and has improper antecedent basis in the limitation 'the vaccine' (see last line), because there is no earlier recitation of 'a vaccine' in this independent claim.

(b) Claims 1 and 3 are indefinite and/or inconsistent in scope. Claim 3, as amended, is indefinite and confusing in the limitation: 'the heterologous antigen induces an immune response against a pathogenic microorganism in said subject to whom the vaccine is administered'. Claim 3 depends from claim 1, which recites that the recombinant bacterium 'elicits an immune response against the heterologous antigen in a subject to whom the vaccine is administered orally'. Does it

mean that two separate immune responses are elicited by the vaccine of claim 3?

(c) Analogous criticism applies to claims 4 and 5.

(d) Claim 3 is further vague and indefinite, because it is improperly broadening in scope with regard to the vaccine administration. Claim 3 depends from claim 1 wherein the vaccine administration in a subject is limited to oral administration. However, in the dependent claim 3, the vaccine administration encompasses non-oral administration.

(e) Claim 25 is indefinite in that it depends from a canceled claim.

(f) Claim 36 is indefinite and/or incorrect in the limitation: 'a surface glycoprotein of *Leishmania* parasite'. Claim 36 depends from the amended claim 7, wherein the recited heterologous antigen is limited to a viral or bacterial antigen and does not encompass a parasitic antigen.

(g) New claim 36 is indefinite, incorrect and has improper antecedence in the limitation: 'the heterologous antigens is' [Emphasis added]. Claim 36 depends from claim 7, which does not recite 'heterologous antigens'.

(h) New claim 37 is indefinite, confusing, and improperly broadening in scope in the limitation: 'said homologous expression or secretion signal is an expression vector for *Lactobacilli*'. Claim 37 depends from claim 12, which includes the limitation: 'the recombinant *Lactobacillus plantarum* comprises a homologous expression or secretion signal', i.e., *Lactobacillus plantarum* expression signal or *Lactobacillus plantarum* secretion signal. The dependent claim 37 improperly encompasses the expression or secretion signal as an expression vector for the broader *Lactobacilli*'.

(i) New claims 39-41 have improper antecedent basis in the limitation: 'said ..... strain or 'said strain'. Claims 39-41 depend directly or indirectly from the amended claim 13, which does not include the limitation of a 'strain'.

(j) Claims 39-41 are indefinite in that these claims have improper antecedent basis in the limitation: 'the vaccinated individual'. Claims 39-41 depend directly or indirectly from claim 13, which does not recite a 'vaccinated individual'.

(k) New claim 42 is confusing and vague in the limitation: '*Lactobacillus plantarum* ..... is **a** recombinant *Lactobacillus plantarum* 256' [Emphasis added]. Does it mean that there are more than one recombinant strains of *Lactobacillus plantarum* 256?

(l) Claim 20 is indefinite and confusing in the limitation: 'non-human foodstuff', because it is unclear what is encompassed in this limitation. Does it mean that the recited foodstuff is of animal origin, for example, poultry or beef foodstuff, or does it mean that the recited foodstuff is a foodstuff for non-humans, for example, animal feed?

(m) New claim 45 is vague and indefinite in the limitation: 'antigen is expressed on the cell surface', because it is not clear the surface of which cell, or the cell surface of what element, is the antigen expressed on.

(n) Analogous criticism applies to new claims 33 and 34.

(o) Claim 24 is indefinite and confusing in the limitation 'intracellular ..... exposure of a heterologous antigen', because it is unclear what is encompassed in the process of 'exposure' of the antigen.

(p) Claim 5 is indefinite and/or incorrect in the limitation '*carnii*'. Neither the specification nor the art recognizes such a limitation.

(q) Claims 2-10, 12, 13, 15-17, 21 and 31-46, which depend directly or indirectly from claim 1, 18 or 20, are also rejected as being indefinite because of the indefiniteness identified above in the base claim.

Rejection(s) under 35 U.S.C. § 102

46) Claims 1-5, 7-10, 12, 13, 15-18, 20-25, 32-34 and 36-46 are rejected under 35 U.S.C § 102(b) as being anticipated by Shaw *et al.* (*Immunology* 100: 510-518, August 2000 – Applicants' IDS).

Instant claims are granted the effective filing date of the instant application, 06/25/02, because of the lack of descriptive support for the claim limitation 'a subject to whom the vaccine is administered' in prior applications.

It is noted that the specification describes that *Lactobacillus plantarum* 256 is found in silage.

Shaw *et al.* taught a recombinant *Lactobacillus plantarum* 256, modified to comprise an expression vector having a lactobacillary secretion signal and a heterologous TTFC protein encoding sequence, which expresses the heterologous TTFC protein antigen or immunogen as an intracellular or a surface-exposed protein. The strain is known to persist in the GI tract for about 12 days (see first full paragraph in right column on page 511). An oral vaccine comprising the recombinant *Lactobacillus platarum* 256 and NaHCO3 (i.e., pharmacologically acceptable carrier) was used for

oral immunization of mice, in whom the vaccine elicited a significant TTFC-specific IgG immune response following oral administration. See 'Summary', 'Materials and Methods' on page 511; Tables 1 and 2; subsection 'Immunization' in left column of page 512; pages 515 and 516; and Figure 4. That the prior art recombinant *Lactobacillus plantarum* 256 from silage qualifies as a bacterium of non-human origin is inherent from the teachings of Shaw *et al.*

Claims 1-5, 7-10, 12, 13, 15-18, 20-25, 32-34 and 36-46 are anticipated by Shaw *et al.*

47) Claims 1, 8, 16, 18, 33 and 42 are rejected under 35 U.S.C. § 102(b) as being anticipated by Maassen (*J. Immunol. Methods* 223: 131-136, February 1999, already of record).

Instant claims are granted the effective filing date of the instant application, 06/25/02, because of the lack of descriptive support for the claim limitation, 'a subject to whom the vaccine administered', in prior applications.

The limitation 'oral vaccine' in the amended claim 1 represents the intended use of the claimed recombinant *L. plantarum* and is not given patentable weight. It is further noted that the term 'oral vaccine' is defined at lines 19 and 20 of page 7 of the specification as any vaccine that is suited, adapted, intended and/or formulated for oral delivery. The instant specification at page 15, first paragraph, expressly describes that the 'antigen is able to elicit or stimulate an immune response'. It is noted that the specification describes that *Lactobacillus plantarum* 256 is found in silage.

Maassen taught that she/he developed genetically engineered lactobacilli as oral vaccines wherein recombinant lactobacilli express microbial heterologous antigens on the cell surface and induce antibodies in mice on oral administration (see page 131; section 2.3; and page 135). One such product was a recombinant *Lactobacillus plantarum* 256 transformed with a plasmid encoding tetanus toxin fragment C, pLP401-TTFC (see section 3.5). Maassen's recombinant *Lactobacillus plantarum* 256 is the same *Lactobacillus plantarum* 256 strain that is claimed in claim 16. That the prior art recombinant *Lactobacillus plantarum* 256 from silage qualifies as a bacterium of non-human origin is inherent from the teachings of Maassen. The limitation regarding the elicitation of an immune response against the heterologous antigen in a subject to whom the recombinant *Lactobacillus plantarum* is administered, represents the functional limitation. As long as the prior art taught a recombinant *Lactobacillus plantarum* 256 expressing a heterologous antigen

intracellularly and/or on its surface, such a recombinant *Lactobacillus plantarum* anticipates the claim(s). Maassen's (1996) product meets the instantly claimed product structurally. The limitation on the elicitation of an immune response against the heterologous antigen in a subject to whom the vaccine administered, is viewed as an inherent function that is inseparable from the prior art product. Products that are identical in structure or composition cannot have mutually exclusive properties. Such products and their properties are inseparable. Therefore, if the prior art taught the identical product, the property Applicant discloses and/or claims is necessarily present. *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Although Maassen is silent about the one or more properties recited in the instant claims, the prior art recombinant *Lactobacillus plantarum* 256 expressing the heterologous antigen intracellularly is viewed as the same as the Applicants' recombinant *Lactobacillus plantarum* 256 expressing the heterologous antigen on the surface, because the prior art product meets all the structural limitations of the claimed product. Since the prior art recombinant *Lactobacillus plantarum* 256 expressing a heterologous antigen is structurally the same as the recombinant *Lactobacillus plantarum* recited in the instant claims, it is expected to have the same intrinsic properties as that of the Applicants' recombinant *Lactobacillus plantarum*, i.e., the ability to elicit an immune response against the heterologous antigen in a subject to whom the vaccine is administered. MPEP 2112.01 [R-3] states that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). "When the PTO shows a sound basis for believing that the products of the applicant and the prior art are the same, the Applicant has the burden of showing that they are not." *In re Spada*, 911 F.2d 705, 709, 15 USPQ2d 1655, 1658 (Fed. Cir. 1990). Since the Office does not have the facilities for examining and comparing Applicants' recombinant *Lactobacillus plantarum* expressing a heterologous antigen with the prior art recombinant *Lactobacillus plantarum* expressing a heterologous antigen on its surface for functional properties, the burden is on the Applicants to show a novel or an unobvious difference between the instantly claimed product and the prior art product. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzerald et al.*, 05 USPQ 594.

Claims 1, 8, 16, 33 and 42 are anticipated by Maassen.

48) Claims 1-7, 9, 10, 12, 13, 15, 18, 22-25, 31, 32 and 35-41 are rejected under 35 U.S.C. § 102(b) as being anticipated by Wells *et al.* (*Antonie van Leeuwenhoek* 70: 317-330, 1996).

The limitation 'oral vaccine' in claim 1, the limitation 'for use in a vaccine' in claim 23, or the limitation 'for use in a method of prophylaxis or treatment of the human or animal body' in claim 25 represents the intended use of the recited recombinant *L. plantarum* and is not given any patentable weight. It is noted that the instant specification at page 15, first paragraph, expressly describes that the 'antigen is able to elicit or stimulate an immune response'.

Wells *et al.* taught a recombinant *L. plantarum,* which expresses a *S. pyogenes* and rotaviral antigen or a HIV-1 viral envelope protein antigen intracellularly and persists in the GI tract for approximately (i.e., $\pm$ 10) 9-12 days. See page 323; and Tables 2 and 1. Wells' recombinant *L. plantarum* comprises an expression vector containing *cbh* promoter or pGIP plasmid (see Table 2). The limitation 'elicits an immune response against the heterologous antigen in a subject to whom the vaccine is administered' is viewed as a functional limitation representing the intrinsic property inseparable from the prior art recombinant *L. plantarum.* That rotavirus is a viral pathogen of the GI tract and *S. pyogenes* is a bacterial pathogen entering the body mucosally via the mucosal or oral route is inherent from the teachings of Wells *et al.* in light of what is well known in the art. Although Wells *et al.* are silent about the one or more properties recited in the instant claims, the prior art recombinant *Lactobacillus plantarum* expressing the heterologous antigen intracellularly is viewed as the same as the Applicants' recombinant *Lactobacillus plantarum* expressing the heterologous antigen intracellularly, because the prior art product meets all the structural limitations of the claimed product. Since the prior art recombinant *Lactobacillus plantarum* expressing a heterologous antigen is structurally the same as the recombinant *Lactobacillus plantarum* recited in the instant claims, it is expected to have the same intrinsic properties as that of the Applicants' recombinant *Lactobacillus plantarum*, i.e., the ability to elicit an immune response against the heterologous antigen in a subject to whom the vaccine is administered. MPEP 2112.01 [R-3] states that where the claimed and prior art products are identical or substantially identical in structure or composition, or are produced by identical or substantially identical processes, a *prima facie* case of either anticipation or obviousness has been established. *In re Best*, 562 F.2d 1252, 1255, 195 USPQ 430, 433 (CCPA 1977). Since the Office does not have the facilities for examining and comparing

Applicants' recombinant *Lactobacillus plantarum* expressing a heterologous antigen with the prior art recombinant *Lactobacillus plantarum* expressing a heterologous antigen intracellularly for functional properties, the burden is on the Applicants to show a novel or an unobvious difference between the instantly claimed product and the prior art product. See *In re Best*, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and *In re Fitzerald et al.*, 05 USPQ 594.

Claims 1-7, 9, 10, 12, 13, 15, 18, 22-25, 31, 32 and 35-41 are anticipated by Wells *et al.*

Remarks

49) Claims 1-10, 12, 13, 15-18, 20-25 and 31-46 stand rejected.

50) Applicants' amendments necessitated the new ground(s) of rejections presented in this Office action. **THIS ACTION IS MADE FINAL.** Applicants are reminded of the extension of time policy as set forth in 37 C.F.R 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

51) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center, which receives transmissions 24 hours a day and 7 days a week. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The Fax number for submission of amendments, responses or papers is (571) 273-8300.

52) Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAG or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.Mov. Should you have questions on access to the Private PAA system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

53) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (571) 272-0854. A message may be left on the Examiner's voice mail system. The Examiner can normally be reached on Monday to Friday from 7.15 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (571) 272-0864.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (571) 272-1600.

January, 2006

S. DEVI, PH.D.
PRIMARY EXAMINER